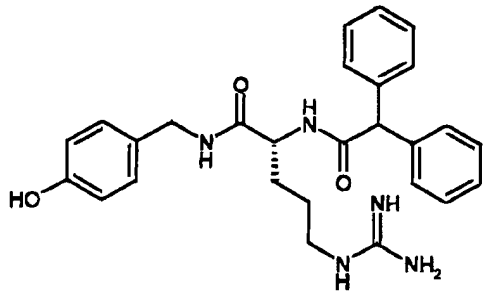
(iv) doses of PDE5 inhibitor we observe a maximal potentiation of ICP, the finding that the ICP can be further potentiated beyond this maximal PDE5 inhibitor mediated is highly unexpected. This illustrates that there are a number of clinical benefits of concomitant administration of a PDE5 inhibitor and a NPY Y1 receptor inhibitor over PDE5 inhibitor therapy alone. These include increased efficacy and opportunities to treat MED subgroups that do not respond to PDE5 inhibitor therapy.

NPY Y1 receptor antagonists and PDE5 or combinations of the two, have no significant effect on un-stimulated ICP i.e. they do not directly induce an increase in ICP in the absence of sexual drive/arousal. This is highly advantageous as the only other marketed therapy for MED which requires sexual stimulation to work is sildenafil thus the present invention provides a viable alternative oral therapy to sildenafil and all other PDE5 alone based drugs.

NPYi - ANIMAL MODEL EXAMPLES

Compounds used in Examples 1 to 6:

NPY receptor antagonist: BIBP 3226

 Chiral	NPY Y1 antagonist Available from Dr Karl Thomae GmbH (Formerly Boehringer Ingelheim Pharma KG) BIBP-3226 WO-09417035

BIBP3226 has an IC50 against human native NPY Y1 = 7nM, selectivity for NPY Y1 (human) over NPY Y5 (human) is greater than 1000, and NPY Y1 selectivity over NPY Y2 (human) is greater than 1000. (See Rudolf *et al* (1994) and Jacques *et al* (1995)).

PDE5i:3-ethyl-5-{5-[4-ethylpiperzino)sulphonyl-2-propoxyphenyl}-2-(2-pyridylmethyl)-6,7-dihydro-2H-pyrazolo[4,3-*d*]pyrimidin-7-one also known as 3-ethyl-5-[5-(4-ethylpip razin-1-ylsulphonyl)-2-n-propoxyphrenyl]-2-(pyridin-2-yl)methyl-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (see WO98/491066). IC50 against human native

PDE5=1.1nM, selectivity for PDE5 over PDE3 (both on native human) is greater than 90,000 and selectivity over PDE4 is 18,545.

All potency and selectivity values quoted are with respect to the human native enzyme (see assays herein).

Example 1. Inhibition of NPY Y1 receptors dose-dependently potentiates nerve stimulated increases in intracavernosal pressure in anaesthetised rabbit model of erection.

Submaximal increases in intracavernosal pressure (ICP) induced by nerve-stimulation were significantly increased in the presence of increasing doses of a selective NPY Y1 receptor antagonist (BIBP3226) (iv bolus). The increase became significant at doses of 30μg/kg and above. The maximal potentiation (circa 127%) was observed at 30μg/kg. Data is expressed as the percentage (%) increase, compared to control stimulated increases. Values are expressed as mean ± s.e.mean. * P<0.05, Students t-test unpaired compared with control increases. (See Figure 1)

There were no major effects of NPY Y1 receptor antagonism on basal/un-stimulated intracavernosal pressure.

Example 2. PDE5 inhibition significantly increases the efficacy of PDE5 inhibitor to enhance penile erection in an anaesthetised rabbit model of erection.

Intravenous administration of a selective PDE5 inhibitor (1 mg/kg) significantly enhanced nerve-stimulated increases in ICP by 133±22% compared to control increases. Data is expressed as percentage increase in ICP over control increases. Values are expressed as mean ± s.e.mean. * P<0.01, Students t-test unpaired compared with control increases. (See Figure 2)

There were no effects of PDE5 inhibition on basal/un-stimulated intracavernosal pressure.